UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

NOTICE OF ALLOWANCE AND FEE(S) DUE

22428 7590 05/01/2009

FOLEY AND LARDNER LLP
SUITE 500
3000 K STREET NW
WASHINGTON, DC 20007

EXAMINER	
SWOPE, SHERIDAN	
ART UNIT	PAPER NUMBER
1652	

DATE MAILED: 05/01/2009

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/507,506	12/13/2004	Moritz Rossner	085449-0150	6374

TITLE OF INVENTION: NOVEL METHOD FOR DETECTING AND ANALYZING PROTEIN INTERACTIONS IN VIVO

APPLN. TYPE	SMALL ENTITY	ISSUE FEE DUE	PUBLICATION FEE DUE	PREV. PAID ISSUE FEE	TOTAL FEE(S) DUE	DATE DUE
nonprovisional	NO	$1510	$0	$1510	$1510	08/03/2009

THE APPLICATION IDENTIFIED ABOVE HAS BEEN EXAMINED AND IS ALLOWED FOR ISSUANCE AS A PATENT. PROSECUTION ON THE MERITS IS CLOSED. THIS NOTICE OF ALLOWANCE IS NOT A GRANT OF PATENT RIGHTS. THIS APPLICATION IS SUBJECT TO WITHDRAWAL FROM ISSUE AT THE INITIATIVE OF THE OFFICE OR UPON PETITION BY THE APPLICANT. SEE 37 CFR 1.313 AND MPEP 1308.

THE ISSUE FEE AND PUBLICATION FEE (IF REQUIRED) MUST BE PAID WITHIN THREE MONTHS FROM THE MAILING DATE OF THIS NOTICE OR THIS APPLICATION SHALL BE REGARDED AS ABANDONED. THIS STATUTORY PERIOD CANNOT BE EXTENDED. SEE 35 U.S.C. 151. THE ISSUE FEE DUE INDICATED ABOVE DOES NOT REFLECT A CREDIT FOR ANY PREVIOUSLY PAID ISSUE FEE IN THIS APPLICATION. IF AN ISSUE FEE HAS PREVIOUSLY BEEN PAID IN THIS APPLICATION (AS SHOWN ABOVE), THE RETURN OF PART B OF THIS FORM WILL BE CONSIDERED A REQUEST TO REAPPLY THE PREVIOUSLY PAID ISSUE FEE TOWARD THE ISSUE FEE NOW DUE.

HOW TO REPLY TO THIS NOTICE:

I. Review the SMALL ENTITY status shown above.

If the SMALL ENTITY is shown as YES, verify your current SMALL ENTITY status:

A. If the status is the same, pay the TOTAL FEE(S) DUE shown above.

B. If the status above is to be removed, check box 5b on Part B - Fee(s) Transmittal and pay the PUBLICATION FEE (if required) and twice the amount of the ISSUE FEE shown above, or

If the SMALL ENTITY is shown as NO:

A. Pay TOTAL FEE(S) DUE shown above, or

B. If applicant claimed SMALL ENTITY status before, or is now claiming SMALL ENTITY status, check box 5a on Part B - Fee(s) Transmittal and pay the PUBLICATION FEE (if required) and 1/2 the ISSUE FEE shown above.

II. PART B - FEE(S) TRANSMITTAL, or its equivalent, must be completed and returned to the United States Patent and Trademark Office (USPTO) with your ISSUE FEE and PUBLICATION FEE (if required). If you are charging the fee(s) to your deposit account, section "4b" of Part B - Fee(s) Transmittal should be completed and an extra copy of the form should be submitted. If an equivalent of Part B is filed, a request to reapply a previously paid issue fee must be clearly made, and delays in processing may occur due to the difficulty in recognizing the paper as an equivalent of Part B.

III. All communications regarding this application must give the application number. Please direct all communications prior to issuance to Mail Stop ISSUE FEE unless advised to the contrary.

IMPORTANT REMINDER: Utility patents issuing on applications filed on or after Dec. 12, 1980 may require payment of maintenance fees. It is patentee's responsibility to ensure timely payment of maintenance fees when due.

PTOL-85 (Rev. 08/07) Approved for use through 08/31/2010.

PART B - FEE(S) TRANSMITTAL

Complete and send this form, together with applicable fee(s), to: Mail **Mail Stop ISSUE FEE**
Commissioner for Patents
P.O. Box 1450
Alexandria, Virginia 22313-1450
or Fax (571)-273-2885

INSTRUCTIONS: This form should be used for transmitting the ISSUE FEE and PUBLICATION FEE (if required). Blocks 1 through 5 should be completed where appropriate. All further correspondence including the Patent, advance orders and notification of maintenance fees will be mailed to the current correspondence address as indicated unless corrected below or directed otherwise in Block 1, by (a) specifying a new correspondence address; and/or (b) indicating a separate "FEE ADDRESS" for maintenance fee notifications.

CURRENT CORRESPONDENCE ADDRESS (Note: Use Block 1 for any change of address)

22428 7590 05/01/2009

FOLEY AND LARDNER LLP
SUITE 500
3000 K STREET NW
WASHINGTON, DC 20007

Note: A certificate of mailing can only be used for domestic mailings of the Fee(s) Transmittal. This certificate cannot be used for any other accompanying papers. Each additional paper, such as an assignment or formal drawing, must have its own certificate of mailing or transmission.

Certificate of Mailing or Transmission

I hereby certify that this Fee(s) Transmittal is being deposited with the United States Postal Service with sufficient postage for first class mail in an envelope addressed to the Mail Stop ISSUE FEE address above, or being facsimile transmitted to the USPTO (571) 273-2885, on the date indicated below.

(Depositor's name)
(Signature)
(Date)

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/507,506	12/13/2004	Moritz Rossner	085449-0150	6374

TITLE OF INVENTION: NOVEL METHOD FOR DETECTING AND ANALYZING PROTEIN INTERACTIONS IN VIVO

APPLN. TYPE	SMALL ENTITY	ISSUE FEE DUE	PUBLICATION FEE DUE	PREV. PAID ISSUE FEE	TOTAL FEE(S) DUE	DATE DUE
nonprovisional	NO	$1510	$0	$1510	$1510	08/03/2009

EXAMINER	ART UNIT	CLASS-SUBCLASS
SWOPE, SHERIDAN	1652	435-007100

1. Change of correspondence address or indication of "Fee Address" (37 CFR 1.363).

❑ Change of correspondence address (or Change of Correspondence Address form PTO/SB/122) attached.

❑ "Fee Address" indication (or "Fee Address" Indication form PTO/SB/47; Rev 03-02 or more recent) attached. **Use of a Customer Number is required.**

2. For printing on the patent front page, list

(1) the names of up to 3 registered patent attorneys or agents OR, alternatively,

(2) the name of a single firm (having as a member a registered attorney or agent) and the names of up to 2 registered patent attorneys or agents. If no name is listed, no name will be printed.

1 _____

2 _____

3 _____

3. ASSIGNEE NAME AND RESIDENCE DATA TO BE PRINTED ON THE PATENT (print or type)

PLEASE NOTE: Unless an assignee is identified below, no assignee data will appear on the patent. If an assignee is identified below, the document has been filed for recordation as set forth in 37 CFR 3.11. Completion of this form is NOT a substitute for filing an assignment.

(A) NAME OF ASSIGNEE (B) RESIDENCE: (CITY and STATE OR COUNTRY)

Please check the appropriate assignee category or categories (will not be printed on the patent) : ❑ Individual ❑ Corporation or other private group entity ❑ Government

4a. The following fee(s) are submitted:

❑ Issue Fee

❑ Publication Fee (No small entity discount permitted)

❑ Advance Order - # of Copies _____

4b. Payment of Fee(s): **(Please first reapply any previously paid issue fee shown above)**

❑ A check is enclosed.

❑ Payment by credit card. Form PTO-2038 is attached.

❑ The Director is hereby authorized to charge the required fee(s), any deficiency, or credit any overpayment, to Deposit Account Number _____ (enclose an extra copy of this form).

5. **Change in Entity Status** (from status indicated above)

❑ a. Applicant claims SMALL ENTITY status. See 37 CFR 1.27.

❑ b. Applicant is no longer claiming SMALL ENTITY status. See 37 CFR 1.27(g)(2).

NOTE: The Issue Fee and Publication Fee (if required) will not be accepted from anyone other than the applicant; a registered attorney or agent; or the assignee or other party in interest as shown by the records of the United States Patent and Trademark Office.

Authorized Signature _____ Date _____

Typed or printed name _____ Registration No. _____

This collection of information is required by 37 CFR 1.311. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 12 minutes to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, Virginia 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, Virginia 22313-1450.

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it displays a valid OMB control number.

UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/507,506	12/13/2004	Moritz Rossner	085449-0150	6374

22428 7590 05/01/2009

FOLEY AND LARDNER LLP
SUITE 500
3000 K STREET NW
WASHINGTON, DC 20007

EXAMINER	
SWOPE, SHERIDAN	
ART UNIT	PAPER NUMBER
1652	

DATE MAILED: 05/01/2009

Determination of Patent Term Adjustment under 35 U.S.C. 154 (b)

(application filed on or after May 29, 2000)

The Patent Term Adjustment to date is 137 day(s). If the issue fee is paid on the date that is three months after the mailing date of this notice and the patent issues on the Tuesday before the date that is 28 weeks (six and a half months) after the mailing date of this notice, the Patent Term Adjustment will be 137 day(s).

If a Continued Prosecution Application (CPA) was filed in the above-identified application, the filing date that determines Patent Term Adjustment is the filing date of the most recent CPA.

Applicant will be able to obtain more detailed information by accessing the Patent Application Information Retrieval (PAIR) WEB site (http://pair.uspto.gov).

Any questions regarding the Patent Term Extension or Adjustment determination should be directed to the Office of Patent Legal Administration at (571)-272-7702. Questions relating to issue and publication fee payments should be directed to the Customer Service Center of the Office of Patent Publication at 1-(888)-786-0101 or (571)-272-4200.

PTOL-85 (Rev. 08/07) Approved for use through 08/31/2010.

Notice of Allowability	Application No.	Applicant(s)	
	10/507,506	ROSSNER ET AL.	
	Examiner	Art Unit	
	SHERIDAN SWOPE	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address--

All claims being allowable, PROSECUTION ON THE MERITS IS (OR REMAINS) CLOSED in this application. If not included herewith (or previously mailed), a Notice of Allowance (PTOL-85) or other appropriate communication will be mailed in due course. **THIS NOTICE OF ALLOWABILITY IS NOT A GRANT OF PATENT RIGHTS.** This application is subject to withdrawal from issue at the initiative of the Office or upon petition by the applicant. See 37 CFR 1.313 and MPEP 1308.

1. ☒ This communication is responsive to *April 23, 2009*.

2. ☒ The allowed claim(s) is/are *123 and 125-127*.

3. ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
   a) ☒ All b) ☐ Some* c) ☐ None of the:
      1. ☒ Certified copies of the priority documents have been received.
      2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
      3. ☐ Copies of the certified copies of the priority documents have been received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

   * Certified copies not received: _____.

Applicant has THREE MONTHS FROM THE "MAILING DATE" of this communication to file a reply complying with the requirements noted below. Failure to timely comply will result in ABANDONMENT of this application.
THIS THREE-MONTH PERIOD IS NOT EXTENDABLE.

4. ☐ A SUBSTITUTE OATH OR DECLARATION must be submitted. Note the attached EXAMINER'S AMENDMENT or NOTICE OF INFORMAL PATENT APPLICATION (PTO-152) which gives reason(s) why the oath or declaration is deficient.

5. ☐ CORRECTED DRAWINGS (as "replacement sheets") must be submitted.
   (a) ☐ including changes required by the Notice of Draftsperson's Patent Drawing Review (PTO-948) attached
      1) ☐ hereto or 2) ☐ to Paper No./Mail Date _____.
   (b) ☐ including changes required by the attached Examiner's Amendment / Comment or in the Office action of Paper No./Mail Date _____.

   Identifying indicia such as the application number (see 37 CFR 1.84(c)) should be written on the drawings in the front (not the back) of each sheet. Replacement sheet(s) should be labeled as such in the header according to 37 CFR 1.121(d).

6. ☐ DEPOSIT OF and/or INFORMATION about the deposit of BIOLOGICAL MATERIAL must be submitted. Note the attached Examiner's comment regarding REQUIREMENT FOR THE DEPOSIT OF BIOLOGICAL MATERIAL.

Attachment(s)

1. ☐ Notice of References Cited (PTO-892)
2. ☐ Notice of Draftperson's Patent Drawing Review (PTO-948)
3. ☒ Information Disclosure Statements (PTO/SB/08), Paper No./Mail Date 0409
4. ☐ Examiner's Comment Regarding Requirement for Deposit of Biological Material
5. ☐ Notice of Informal Patent Application
6. ☐ Interview Summary (PTO-413), Paper No./Mail Date _____ .
7. ☒ Examiner's Amendment/Comment
8. ☒ Examiner's Statement of Reasons for Allowance
9. ☐ Other _____.

DETAILED ACTION

Applicants' Petition and Request for Continuing Examination of April 23, 2009, in response to the Notice of Allowability mailed January 9, 2009, is acknowledged. It is acknowledged that no claims have been cancelled, amended, or added since Applicants' filing of September 30, 2008. The Notice of Allowability mailed January 9, 2009 and is replaced with the Notice of Allowability below.

Information Disclosure Statement

The Information Disclosure Statement filed April 23, 2009 has been considered.

Examiner's Amendment

An examiner's amendment to the record appears below. Should the changes and/or additions be unacceptable to Applicant, an amendment may be filed as provided by 37 CFR 1.312. To ensure consideration of such an amendment, it MUST be submitted no later than the payment of the issue fee.

Claims

Cancel Claims 61-122 and 124.

Replace Claims 123 and 125-127 with the following.

123. A method of detecting and analyzing protein interactions in a cell, which comprises the steps:

a) expressing in the cell

a1) a first fusion protein comprising a first interaction partner and a part of the 27 kDa NIa protease of tobacco etch virus, wherein the part of the NIa protease alone does not have proteolytic activity, and

a2) a second fusion protein comprising a second interaction partner and another part of said NIa protease, wherein said another part of the NIa protease alone does not have proteolytic activity, and

a3) a reporter protein, whose reporter activity can be activated or inactivated by proteolysis,

b) reconstituting the functional NIa protease activity via interaction of said first and second interaction partners,

c) detecting and analyzing activation of the proteolysis-activatable or inactivation of the proteolysis-inactivatable reporter protein by the reconstituted functional NIa protease of step b),

wherein said reporter protein is selected from the group consisting of recombinases, transcription activators, fluorescent proteins, luciferases, beta-galactosidase, alkaline phosphatases, beta-lactamase, proteins and enzymes conferring resistance to cytotoxic substances or minimal media, cytotoxic or pro-apoptotic proteins, and proteins altering the growth or morphology of the cell in which they are expressed; and

wherein the part of the NIa protease in a1) and the part of the NIa protease in a2) are generated by dividing the functional NIa protease at a position between amino acids 60 and 80, wherein the NIa protease comprises an amino acid sequence having a catalytic triade comprising histidine at position 46, aspartate at position 81 and cysteine at position 151.

125. A method of detecting and analyzing protein interactions in a cell, which comprises the steps:

a) expressing in the cell

a1) a first fusion protein comprising a first interaction partner and a part of the 27 kDa NIa protease of tobacco etch virus, wherein the part of the NIa protease alone does not have proteolytic activity, and

a2) a second fusion protein comprising a second interaction partner and another part of said NIa protease, wherein said another part of the NIa protease alone does not have proteolytic activity, and

a3) a reporter protein, whose reporter activity can be activated or inactivated by proteolysis,

b) reconstituting the functional NIa protease activity via interaction of said first and second interaction partners,

c) detecting and analyzing activation of the proteolysis-activatable or inactivation of the proteolysis-inactivatable reporter protein by the reconstituted functional NIa protease of step b),

wherein said reporter protein is selected from the group consisting of recombinases, transcription activators, fluorescent proteins, luciferases, beta-galactosidase, alkaline phosphatases, beta-lactamase, proteins and enzymes conferring resistance to cytotoxic substances or minimal media, cytotoxic or pro-apoptotic proteins, and proteins altering the growth or morphology of the cell in which they are expressed; and

wherein the part of the NIa protease in a1) and the part of the NIa protease in a2) are the NIa protease fragments Gly1-Thr70 and Thr71-Gly243, respectively, wherein the NIa protease comprises an amino acid sequence having a catalytic triade comprising histidine at position 46, aspartate at position 81 and cysteine at position 151.

126. A method of detecting and analyzing protein interactions in a cell, which comprises the steps:

a) expressing in the cell

a1) a first fusion protein comprising a first interaction partner and a part of the 27 kDa NIa protease of tobacco etch virus, wherein the part of the NIa protease alone does not have proteolytic activity, and

a2) a second fusion protein comprising a second interaction partner and another part of said NIa protease, wherein said another part of the NIa protease alone does not have proteolytic activity, and

a3) a reporter protein, whose reporter activity can be activated or inactivated by proteolysis,

b) reconstituting the functional NIa protease activity via interaction of said first and second interaction partners,

c) detecting and analyzing activation of the proteolysis-activatable or inactivation of the proteolysis-inactivatable reporter protein by the reconstituted functional NIa protease of step b),

wherein said reporter protein is selected from the group consisting of recombinases, transcription activators, fluorescent proteins, luciferases, beta-galactosidase, alkaline phosphatases, beta-lactamase, proteins and enzymes conferring resistance to cytotoxic substances or minimal media, cytotoxic or pro-apoptotic proteins, and proteins altering the growth or morphology of the cell in which they are expressed; and

wherein the part of the NIa protease in a1) and the part of the NIa protease in a2) are the NIa protease fragements Gly1-Thr118 and Lys119-Gly243, respectively, wherein the NIa protease comprises an amino acid sequence having a catalytic triade comprising histidine at position 46, aspartate at position 81 and cysteine at position 151.

127. A method of detecting and analyzing protein interactions in a cell, which comprises the steps:

a) expressing in the cell

a1) a first fusion protein comprising a first interaction partner and a part of the 27 kDa NIa protease of tobacco etch virus, wherein the part of the NIa protease alone does not have proteolytic activity, and

a2) a second fusion protein comprising a second interaction partner and another part of said NIa protease, wherein said another part of the NIa protease alone does not have proteolytic activity, and

a3) a reporter protein, whose reporter activity can be activated or inactivated by proteolysis,

b) reconstituting the functional NIa protease activity via interaction of said first and second interaction partners,

c) detecting and analyzing activation of the proteolysis-activatable or inactivation of the proteolysis-inactivatable reporter protein by the reconstituted functional NIa protease of step b),

wherein said reporter protein is selected from the group consisting of recombinases, transcription activators, fluorescent proteins, luciferases, beta-galactosidase, alkaline phosphatases, beta-lactamase, proteins and enzymes conferring resistance to cytotoxic substances or minimal media, cytotoxic or pro-apoptotic proteins, and proteins altering the growth or morphology of the cell in which they are expressed; and

wherein the part of the NIa protease in a1) and the part of the NIa protease in a2) are the NIa protease fragments Gly1-Thr70 and His61-Gly243, respectively, wherein the NIa protease comprises an amino acid sequence having a catalytic triade comprising histidine at position 46, aspartate at position 81 and cysteine at position 151.

Authorization for this examiner's amendment was given in a telephone interview with Yang Tang on December 29, 2008.

Allowable Subject Matter

Claims 123 and 125-127 are allowed.

The following is an examiner's statement of reasons for allowance:

All allowable claims, Claims 123 and 125-127, are limited to a method of detecting protein/protein interaction by reconstituting the activity of the 27 kDa NIa protease of tobacco etch virus. The recited invention is enabled and is useful. Methods for detecting protein/protein interaction by reconstituting the activity of an enzyme were known in the art (Fields et al, 1989). The 27 kDa NIa protease of tobacco etch virus was also well-known in the art, the virus having been completely sequenced in 1986 (Allison et al) with the NIa protease identified as beginning with Gly^{2038} (GenBank AAA47909, 1993); thus, having His^{46}, Asp^{81}, and Cys^{151} catalytic residues. The teachings of Bazan et al, 1988 suggest that the NIa protease of tobacco etch virus can be divided in the hinge region, residues 90-99, and the activity reconstituted. However, the instant invention is allowable because methods dividing the NIa protease anywhere between

amino acids 60 and 80 or using the NIa protease fragment pairs Gly1-Thr70 and Thr71-Gly243, Gly1-Thr118 and Lys119-Gly243, or Gly1-Thr70 and His61-Gly243 are not anticipated by or obvious over the prior art.

Any comments considered necessary by applicant must be submitted no later than the payment of the issue fee and, to avoid processing delays, should preferably accompany the issue fee. Such submissions should be clearly labeled "Comments on Statement of Reasons for Allowance."

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sheridan L. Swope whose telephone number is 571-272-0943. The examiner can normally be reached on M-F; 9:30-7 EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Nashed can be reached on 571-272-0934. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published application may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on the access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/SHERIDAN SWOPE/
Primary Examiner, Art Unit 1652